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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/961,163	09/21/2001	Katherine E. Fisher	PC10667AGPR	4614

7590 09/08/2004
Gregg C. Benson
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EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/961,163

Applicant(s)

FISHER ET AL.

Examiner

Celine X Qian

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 10-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 9/21/01 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-20 are pending in the application. Claims 10-20 are withdrawn from consideration for being directed to non-elected subject matter. Claims 1-9 are currently pending.

This Office Action is in response to the Amendment filed on 6/8/04.

Response to Amendment

The objection to the specification has been withdrawn in light of Applicant's amendment.

The rejection of claims 1, 2, 4, 6 and 7 under 35 U.S.C. 102 (b) has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 3, 5, and 8 under 35 U.S.C. 103 (a) has been withdrawn in light of Applicant's amendment of the claims.

Claims 1-9 are rejected under 35 U.S.C. 112 1st paragraph for reasons set forth below. The objection to claim 9 is changed to the 112 1st paragraph rejection which is necessitated by the amendment of the claim.

Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 102 (b) for reasons set forth below.

Claims 5 and 8 are rejected under 35 U.S.C. 103 (a) for reasons set forth below.

New Grounds of Rejection Necessitated by Applicant's Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1636

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claims recite "said YTC does not include a yeast selectable marker" as a new limitation. However, this limitation is not supported by the instant specification. The specification discloses that YTC is a DNA molecule comprises a bacterial/mammalian selection marker flanked by recombinogenic arms, and additional genetic elements as well (see page 10 last paragraph). The disclosure of the specification does not exclude the presence of a yeast selection marker. Although the specification discloses one YTC that does not include a yeast selectable marker in the example, it does not support the claimed genus of YTCs wherein a yeast selectable marker is excluded. The fact that one working example in the specification employs a YTC, which does not have a yeast selection marker that applicant may now wish not to have for use in any other YTC as broadly covered by the scope of the new claims after the filing date of the as-filed application, does not provide any legal basis showing that applicant possesses the specific claimed subject matter as claimed in the new claims at the time the invention was made. Thus, this is a new matter rejection. In other words, new or amended claims which introduce elements or limitations such as a subgenus of YTC(s), which exclude a yeast selection marker, and which are not supported by the as-filed disclosure as a whole, violate the written description requirement. See, e.g., *In re Lukach*, 442 F.2d 967, 169

Art Unit: 1636

USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); In re Smith, 458 F.2d 1389,1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads). Therefore, this newly introduced limitation constitutes new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Wattler et al (1999, Biotechnology, Vol. 26, pages 1150-60).

Wattler et al. disclose a lambda KOS vector comprises a stuffer DNA flanked by restriction sites so that the stuffer DNA can be replaced by genomic DNA; an E. coli. origin of replication; an antibiotic resistance gene; a yeast origin of replication (2 μ m); a selectable marker suitable for use in yeast (TRP1 gene); negative selectable markers suitable for use in mammalian cells (HSV-tk gene); a direct repeat of recombinase sequence (loxP) for conversion of the lambda phage vector into E. Coli/yeast shuttle plasmid, said vector also comprises a cos site (see page 1151, 1st col., last paragraph through 3rd col., 2nd paragraph, and Figure 1B). Wattler et al. also disclose a positive selection cassette vector, PGK-neo cassette, comprising a bacterial/mammalian positive selection marker, and recombinant arms that shares homology with the integration site of

Art Unit: 1636

the genomic DNA, which does not have a yeast selection marker (see page 1156, 1st col., 1st paragraph, lines 2-32). Wattler et al. further disclose that the generation of lambda phage library by inserting genomic DNA into KOS vector and replace the stuffer fragment, and infection of a Cre-recombinase expressing bacterial strain to convert the lambda vector into a E. coli/yeast shuttle vector pKOS (see page 1152, 3rd col., 2nd paragraph). This shuttle vector is co-transfected with a positive selection cassette into yeast for inserting the positive selection marker into the genomic DNA by homologous recombination and selection for complementation of yeast strain expressing the yeast selection marker (page 1152, 1st col., 2nd paragraph). The plasmid is recovered from the yeast and transferred into E.coli which allows a further selection by plating on chloramphenicol and ampicillin containing plates using standard procedures, and the gene-targeting vector is finally recovered (page 1152, 2nd col., 1st paragraph). Wattler et al. thus disclose a method of generating a gene-targeting vector for using in murine ES cells by homologous recombination in yeast. Therefore, Wattler et al. disclose the instantly claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wattler et al., in view of Brocard et al. (1997, PNAS, Vol.94, pp.14559-14563).

Art Unit: 1636

The teaching of Wattler et al. is discussed above. However, Wattler et al. do not teach the positive selection cassette vector further comprises loxP or FRT sites flanking the positive selection marker.

Brocard et al. teach a method of spatio-temporally controlled site specific mutagenesis in the mouse by using inducible expression of Cre recombinase and loxP system (see abstract). Brocard et al. teach that by inserting loxP sites flanking the CAT selection marker, the spatio-temporally controlled Cre recombinase effectively removed selection marker and result in expression of lacZ in transgenic mouse (see page 14559, col.2, 2nd paragraph, and page 14560, 2nd col., 2nd paragraph).

It would have been obvious to one of ordinary skill of art to modify the selection vector taught by Wattler by inserting loxP sites to the positive selection cassette vector that flanks the selection marker to achieve temporal regulation in mammalian system as demonstrated by Brocard et al. The ordinary skilled in the art would have been motivated to do so to make a gene-targeting vector that not simply knocks out the gene of interest but can also do it in a controlled manner. The level of skill in the art of molecular cloning is high. Absent evidence from the contrary, one of ordinary skill of art would have reasonable expectation to make the claimed vector. Therefore, the invention would have been prima facie obvious to one of ordinary skill of art at the time the invention was made.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wattler et al., in view of Luo et al. (6,280,937).

Art Unit: 1636

The teaching of Wattler et al. is discussed above. However, Wattler et al. do not teach the positive selection cassette vector further comprises an IRES that allows the translation of the positive selection marker in mammalian cells.

Luo et al. teach a shuttle vector comprising IRES in front of a GFP reporter (see Figure 1). Luo et al. teach that IRES elements functions as initiators of the efficient translation of reading frames, and greatly facilitates the selection of cell expressing peptides at uniformly high levels (see col.8, lines 49-53).

It would have been obvious to one of ordinary skill of art to modified the positive selection cassette taught by Wattler et al. by inserting an IRES in front of the mammalian/bacterial selection marker to ensure the proper expression of the marker in mammalian cells. One of ordinary skill of art would have been motivated to do so because Luo et al. teach that such element greatly facilitates the selection of cell expressing the peptides at high levels. The level of skill in the art of molecular cloning is high. Absent evidence from the contrary, one of ordinary skill of art would have reasonable expectation to make the claimed vector, and use it in the claimed method. Therefore, the invention would have been prima facie obvious to one of ordinary skill of art at the time the invention was made.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1636

This application contains claims 10-20 drawn to an invention nonelected with traverse in response filed on 5/12/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1636

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



DAVE T. NGUYEN
PRIMARY EXAMINER

Celine Qian, Ph.D.